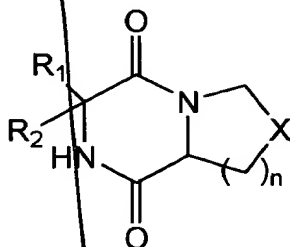


What Is Claimed Is:

1. A compound having the formula:



or a pharmaceutically acceptable salt or hydrate thereof,
wherein

n is an integer from 0 to 3;

X is selected from the group consisting of -S-,
-O-, -NR- and -CH₂-;

R₁ and R₂ are each independently selected from the
group consisting of -H, -OR, -SR, -NRR, NO₂, -CN, -C(O)OR,
-C(O)NRR, -C(NR)NRR, trihalomethyl, (C₁-C₆) alkyl, substituted
(C₁-C₆) alkyl, (C₂-C₆) alkenyl, substituted (C₂-C₆) alkenyl,
(C₂-C₆) alkynyl, substituted (C₂-C₆) alkynyl, (C₅-C₂₀) aryl,
substituted (C₅-C₂₀) aryl, 5-20 membered heteroaryl,
substituted 5-20 membered heteroaryl, (C₆-C₂₆) arylalkyl,
substituted (C₆-C₂₆) arylalkyl, 6-26 membered heteroarylalkyl
and substituted 6-26 membered heteroarylalkyl;

or R₁ and R₂ taken together are -CH₂-(CH₂)_m-CH₂-,
where m is an integer from 0 to 6;

each alkyl, alkenyl, alkynyl, aryl, alkaryl,
heteroaryl or alk-heteroaryl substituent is independently
selected from the group consisting of -OR, -SR, -NRR, -CN,
-NO₂, -C(O)OR, -C(O)NRR, -C(S)NRR, -C(NR)NRR, halogen and
trihalomethyl; and

each R is independently selected from the group
consisting of -H, (C₁-C₆) alkyl, (C₂-C₆) alkenyl, (C₂-C₆)
alkynyl, (C₅-C₂₀) aryl, 5-20 membered heteroaryl, (C₆-C₂₆)
alkaryl and 6-26 membered alk-heteroaryl.

with the provisos that (i) when n is 1 or 2 and X
is -CH₂-, R₁ and R₂ taken together are other than
-CH₂-CH₂-CH₂-CH₂-; and (ii) the compound is not cyclo(Pro-Ala),

cyclo(Pro-Val), cyclo(Pro-Leu), cyclo(Pro-homoLeu), cyclo(Pro-Ile), cyclo(Pro-His), cyclo(Pro-Phe), cyclo(Pro-D-Phe), cyclo(D-Pro-Phe), cyclo(Pro-Tyr), cyclo(Pro-Trp), cyclo(Pro-Lys), cyclo(Pro-Arg) or cyclo(Pro-Asp), where all amino acids are in the L-configuration unless otherwise specified.

2. The compound of Claim 1, wherein X is $-\text{CH}_2-$.

3. The compound of Claim 1, wherein n is 1.

4. The compound of Claim 1, wherein carbon 3 of the 2,5-diketopiperzine ring is the S configuration.

5. The compound of Claim 4, wherein carbon 6 of the 2,5-diketopiperzine ring is the S configuration.

6. The compound of Claim 1, wherein carbon 6 of the 2,5-diketopiperzine ring is the S configuration.

7. The compound of Claim 1, wherein R_1 and R_2 taken together are $-\text{CH}_2-\text{CH}_2-$, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ or $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$.

8. The compound of Claim 1, wherein:

R_1 is $-\text{H}$;

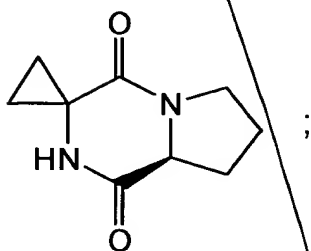
R_2 is $-\text{CH}_2-\text{R}_5$, $-\text{CH}_2-\text{CH}_2-\text{R}_5$ or $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{R}_5$;

R_5 is phenyl, imidazolyl other than imidazol-2-yl, indolyl other than indol-3-yl, $-\text{SR}_6$, $-\text{OR}_6$ or $-\text{NHR}_6$; and

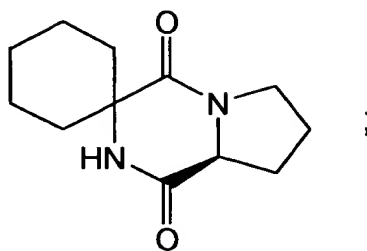
R_6 is $-\text{H}$, (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, $-\text{C}(\text{NH})\text{NH}_2$ or $-\text{C}(\text{S})\text{NH}_2$.

9. The compound of Claim 8, wherein R_5 is N-imidazolyl, $-\text{SR}_{25}$ or $-\text{NHR}_{25}$ and R_{25} is $-\text{H}$, (C_1-C_6) alkyl, $-\text{C}(\text{NH})\text{NH}_2$ or $-\text{C}(\text{S})\text{NH}_2$.

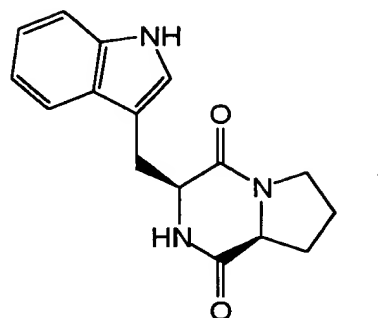
10. The compound of Claim 1 which is selected from the group consisting of:



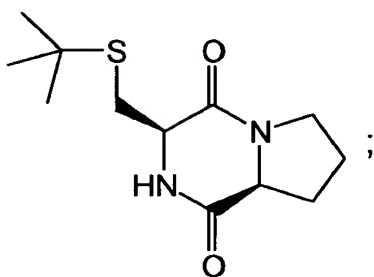
(1a)



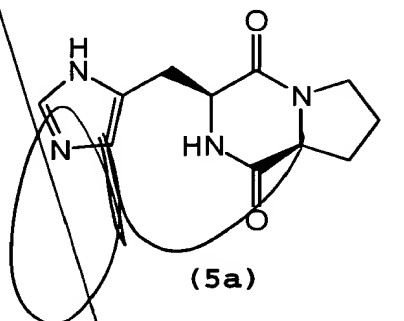
(2a)



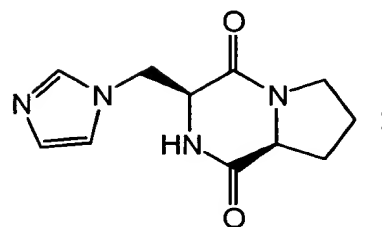
(3a)



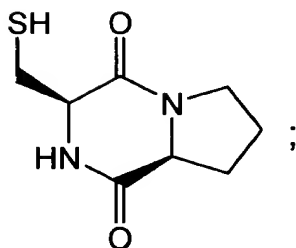
(4a)



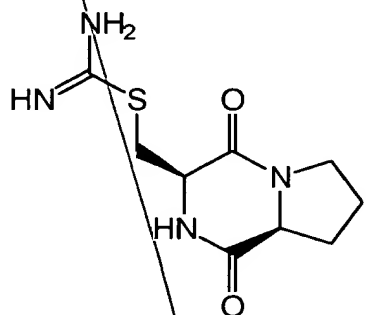
(5a)



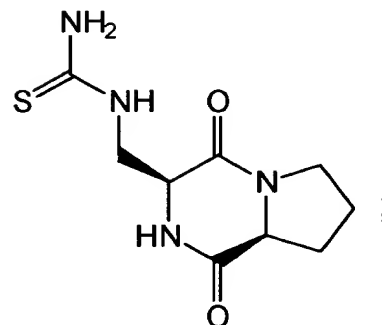
(6a)



(7a)

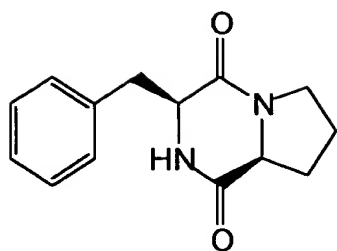


(8a)

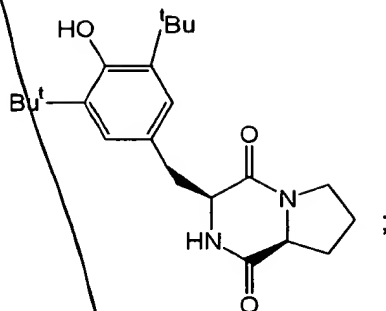


(9a)

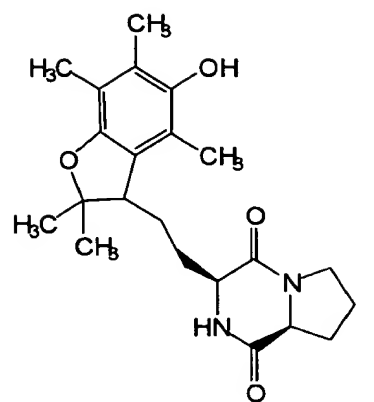
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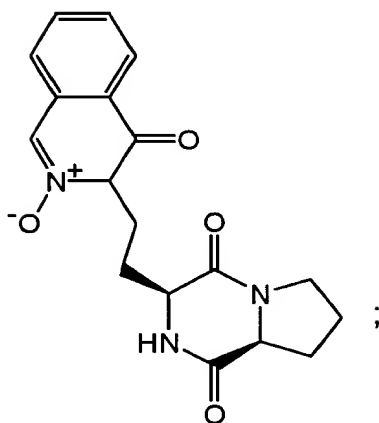
(10a)



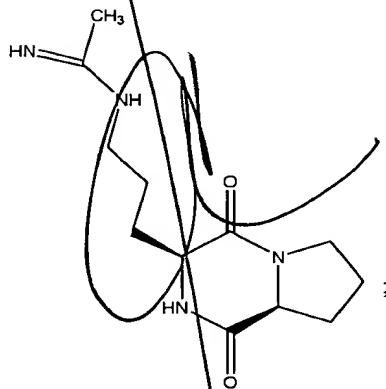
(11a)



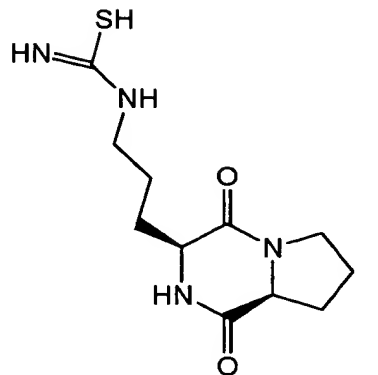
(12a)



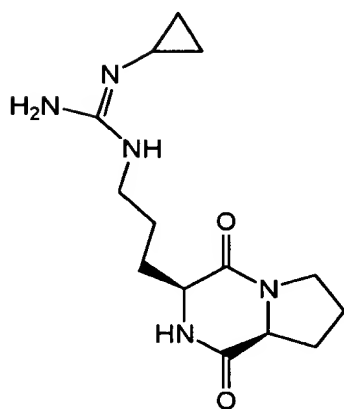
(13a)



(14a)



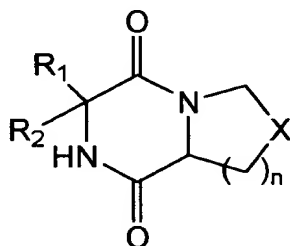
(15a)



(16a)

11. A pharmaceutical composition comprising a compound according to Claim 1 and a pharmaceutically acceptable excipient, carrier or diluent.

12. A method of treating a neurological disorder or CNS injury, said method comprising the step of administering to a subject an effective amount of a compound having the formula:



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

n is an integer from 0 to 3;

X is selected from the group consisting of -S-, -O-, -NR- and -CH₂-;

R₁ and R₂ are each independently selected from the group consisting of -H, -OR, -SR, -NRR, -NO₂, -CN, -C(O)OR, -C(O)NRR, -C(NR)NRR, trihalomethyl, halogen, (C₁-C₆) alkyl, substituted (C₁-C₆) alkyl, (C₂-C₆) alkenyl, substituted (C₂-C₆) alkenyl, (C₂-C₆) alkynyl, substituted (C₂-C₆) alkynyl, (C₅-C₂₀) aryl, substituted (C₅-C₂₀) aryl, 5-20 membered heteroaryl, substituted 5-20 membered heteroaryl, (C₆-C₂₆) alkaryl, substituted (C₆-C₂₆) alkaryl, 6-26 membered alk-heteroaryl and substituted 6-26 membered alk-heteroaryl,

or R₁ and R₂ taken together are -CH₂-(CH₂)_m-CH₂-, where m is an integer from 0 to 6;

each alkyl, alkenyl, alkynyl, aryl, alkaryl, heteroaryl or alk-heteroaryl substituent is independently selected from the group consisting of -OR, -SR, -NRR, -CN, -NO₂, -C(O)OR, -C(O)NRR, -C(S)NRR, -C(NR)NRR, halogen and trihalomethyl; and

each R is independently selected from the group consisting of -H, (C₁-C₆) alkyl, (C₂-C₆) alkenyl, (C₂-C₆)

alkynyl, (C₅-C₂₀) aryl, 5-20 membered heteroaryl, (C₆-C₂₆)
alkaryl and 6-26 membered alk-heteroaryl.

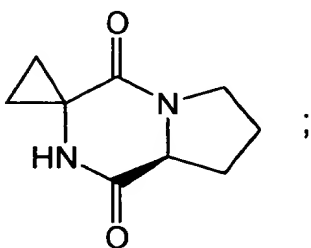
13. The method of Claim 12, wherein the neurological
disorder is caused by brain or spinal cord trauma.

14. The method of Claim 12, wherein both carbons at
positions 3 and 6 of the parent bicyclic 2,5-diketopiperazine
ring are in the S configuration.

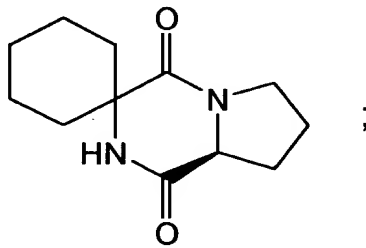
15. The method of Claim 12, wherein X is -CH₂-.

16. The method of Claim 12, wherein n is 1.

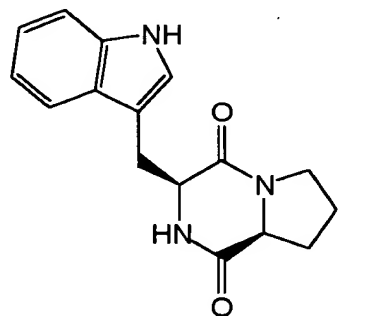
17. The method of Claim 12, wherein said compound is
selected from the group consisting of:



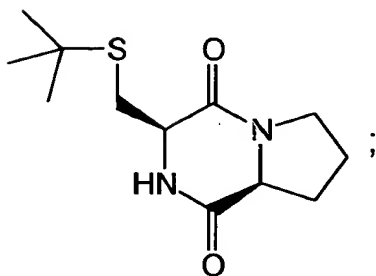
(1a)



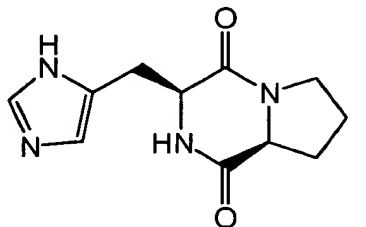
(2a)



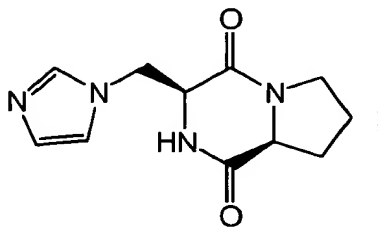
(3a)



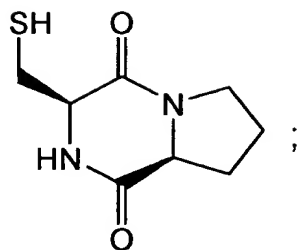
(4a)



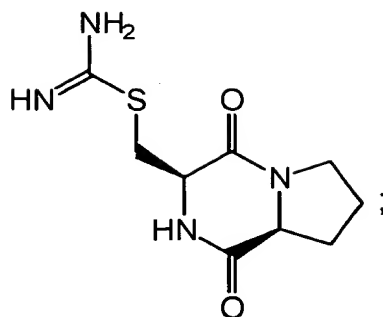
(5a)



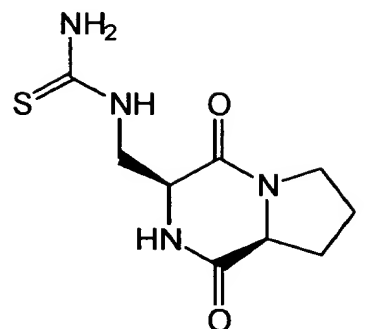
(6a)



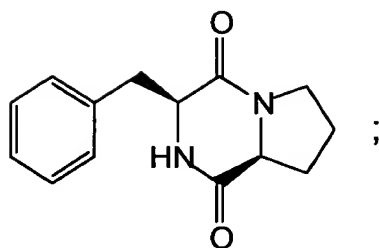
(7a)



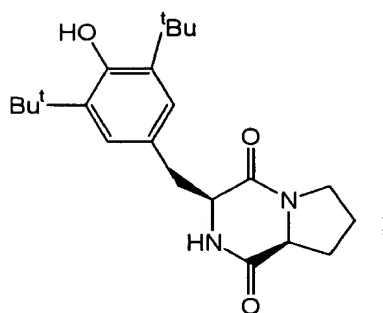
(8a)



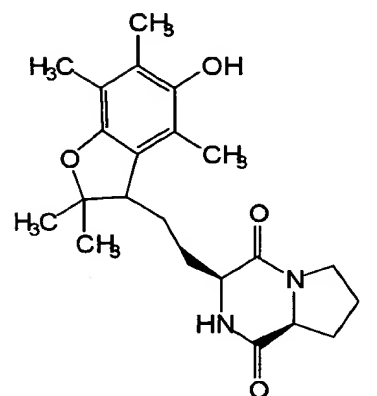
(9a)



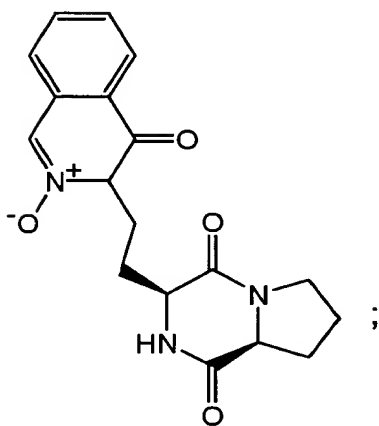
(10a)



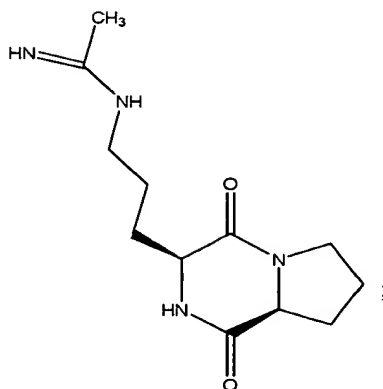
(11a)



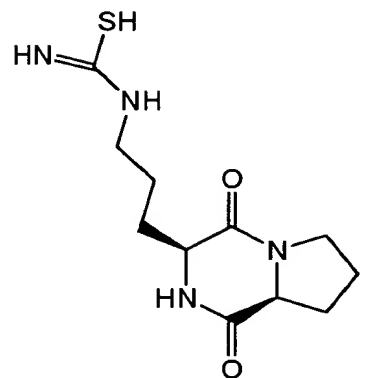
(12a)



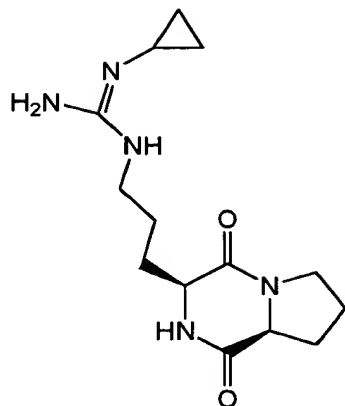
(13a)



(14a)

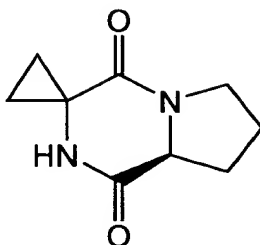


(15a)

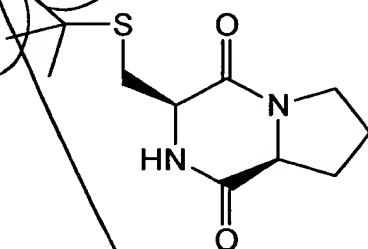


(16a)

18. The method of Claim 12 in which said compound has the following structure:

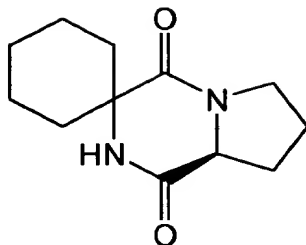


19. The method of Claim 12 in which said compound has the following structure:



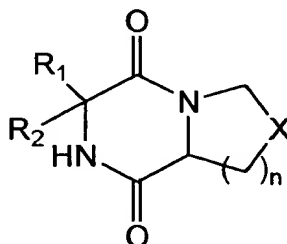
20. The method of Claim 12 in which the neurodegenerative disease is Alzheimer's disease.

21. The method of Claim 12 in which said compound has the following structure:



22. The method of Claim 13 in which the CNS injury is caused by stroke.

23. A method of enhancing cognitive function, said method comprising the step of administering to a subject an effective amount of a compound having the formula:



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

n is an integer from 0 to 3;

X is selected from the group consisting of -S-, -O-, -NR- and -CH₂-;

R₁ and R₂ are each independently selected from the group consisting of -H, -OR, -SR, -NRR, -NO₂, -CN, -C(O)OR, -C(O)NRR, -C(NR)NRR, trihalomethyl, halogen, (C₁-C₆) alkyl, substituted (C₁-C₆) alkyl, (C₂-C₆) alkenyl, substituted (C₂-C₆) alkenyl, (C₂-C₆) alkynyl, substituted (C₂-C₆) alkynyl, (C₅-C₂₀) aryl, substituted (C₅-C₂₀) aryl, 5-20 membered heteroaryl, substituted 5-20 membered heteroaryl, (C₆-C₂₆) alkaryl, substituted (C₆-C₂₆) alkaryl, 6-26 membered alk-heteroaryl and substituted 6-26 membered alk-heteroaryl,

or R₁ and R₂ taken together are -CH₂-(CH₂)_m-CH₂-, where m is an integer from 0 to 6;

each alkyl, alkenyl, alkynyl, aryl, alkaryl, heteroaryl or alk-heteroaryl substituent is independently

selected from the group consisting of -OR, -SR, -NRR, -CN, -NO₂, -C(O)OR, -C(O)NRR, -C(S)NRR, -C(NR)NRR, halogen and trihalomethyl; and

each R is independently selected from the group consisting of -H, (C₁-C₆) alkyl, (C₂-C₆) alkenyl, (C₂-C₆) alkynyl, (C₅-C₂₀) aryl, 5-20 membered heteroaryl, (C₆-C₂₆) alkaryl and 6-26 membered alk-heteroaryl.

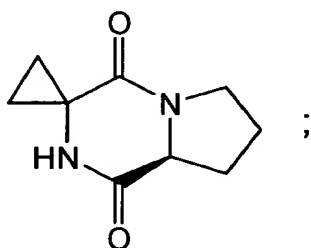
24. The method of Claim 23, wherein the cognitive function is memory.

25. The method of Claim 23, wherein both carbons at positions 3 and 6 of the parent bicyclic 2,5-diketopiperazine ring are in the S configuration.

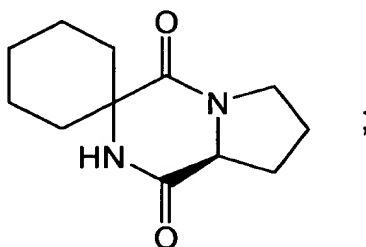
26. The method of Claim 23, wherein X is -CH₂-.

27. The method of Claim 23, wherein n is 1.

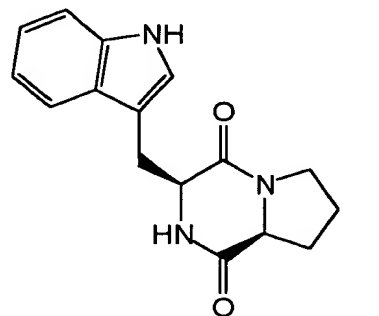
28. The method of Claim 23, wherein said compound is selected from the group consisting of:



(1a)

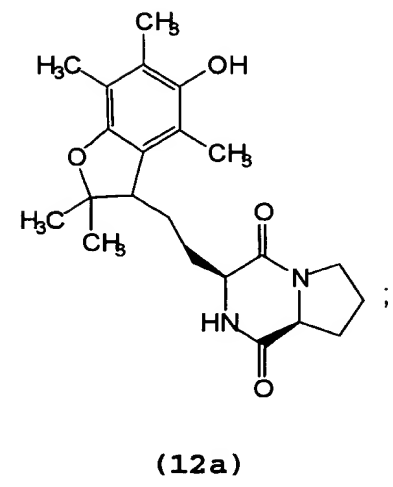
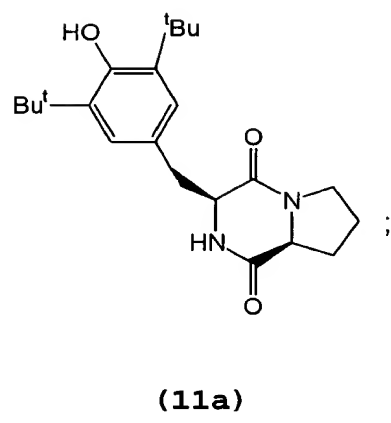
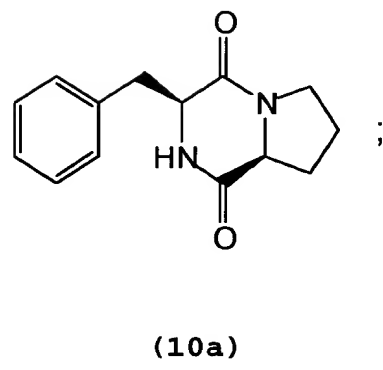
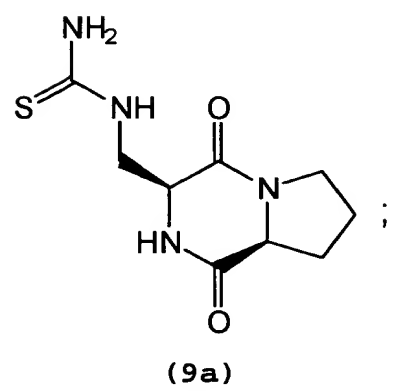
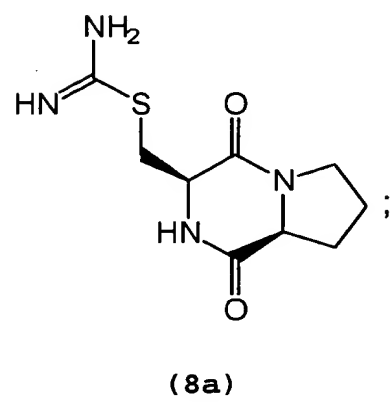
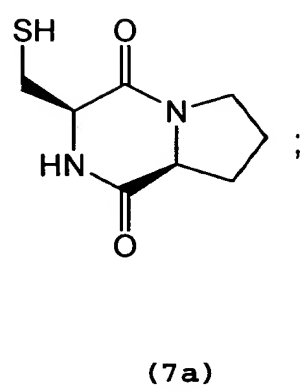
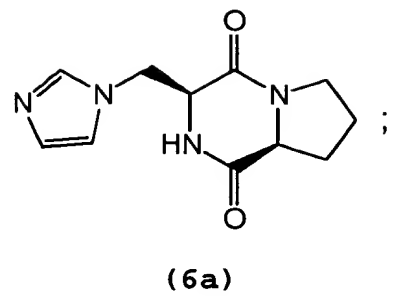
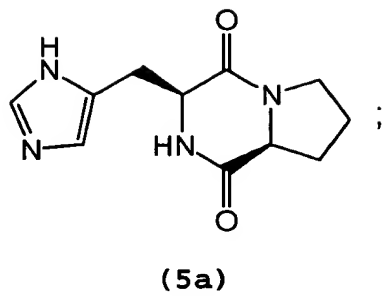
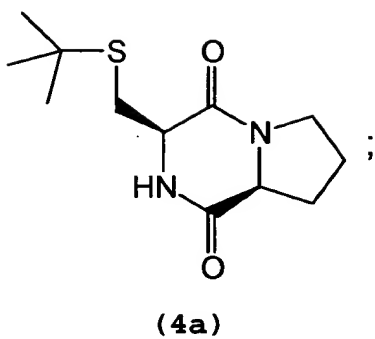


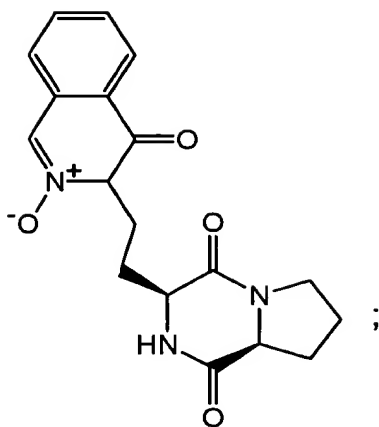
(2a)



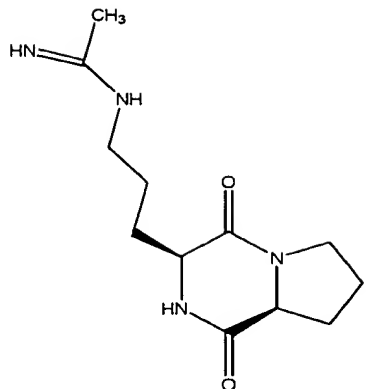
(3a)

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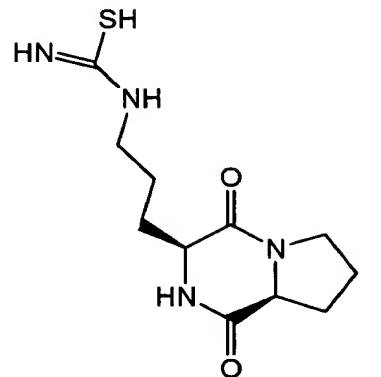




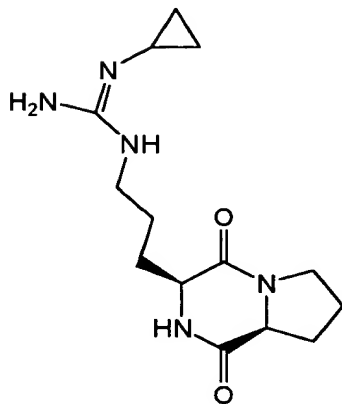
(13a)



(14a)

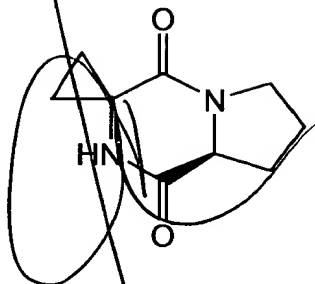


(15a)

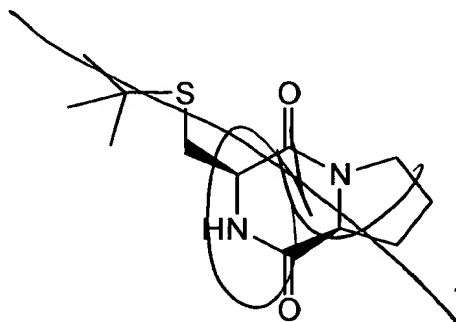


(16a)

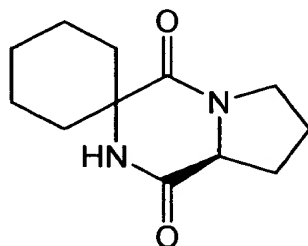
5 29. The method of Claim 23 in which said compound has the following structure:



10 30. The method of Claim 23 in which said compound has the following structure:

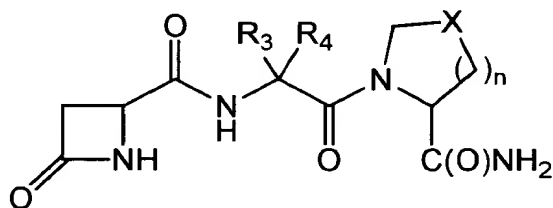


31. The method of Claim 23 in which said compound has
5 the following structure:



32. The method of Claim 23, wherein said compound is
10 administered following acute or chronic brain injury.

33. A compound having the formula:



15 or a pharmaceutically acceptable salt or hydrate thereof,
wherein:

n is an integer from 0 to 3;

X is selected from the group consisting of -S-, -O-, -NR-
and -CH₂-;

20 R₃ and R₄ are each independently selected from the group
consisting of -H, -CN, -C(O)OR', -C(O)NR'R', -C(NR')NR'R',
trihalomethyl, (C₁-C₆) alkyl, substituted (C₁-C₆) alkyl, (C₂-C₆)
alkenyl, substituted (C₂-C₆) alkenyl, (C₂-C₆) alkynyl,
substituted (C₂-C₆) alkynyl, (C₁-C₆) aryl, (C₅-C₂₀) substituted
25 aryl, 5-20 membered heteroaryl, substituted 5-20 membered

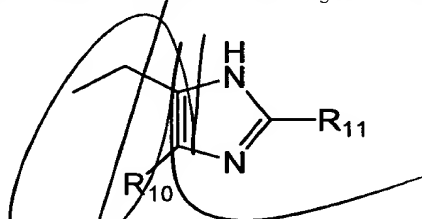
heteroaryl, (C₆-C₂₆) arylalkyl, substituted (C₆-C₂₆) arylalkyl, 6-26 membered heteroarylalkyl and substituted 6-26 membered heteroarylalkyl,

or R₃ and R₄ taken together are -CH₂-(CH₂)_p-CH₂-, where p is an integer from 0 to 6;

each alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl and heteroarylalkyl substituent is independently selected from the group consisting of -R', -OR', -SR', -NR'R', -CN, -NO₂, -C(O)OR', -C(O)NR'R', -C(S)NR'R', -C(NR')NR'R', -NR'-C(NR')-R', -NR'-C(NR')-OR', -NR'-C(NR')-SR', -NR'-C(NR')-NR'R', halogen and trihalomethyl; and

each R' is independently selected from the group consisting of -H, (C₁-C₆) alkyl, (C₂-C₆) alkenyl, (C₂-C₆) alkynyl, (C₅-C₂₀) aryl, (C₆-C₂₆) arylalkyl, 5-20 membered heteroaryl and 6-26 membered heteroarylalkyl,

with the proviso that when n is 1; X is -CH₂-; and one of R₃ or R₄ is -H; then the other of R₃ or R₄ is not:



where R₁₀ is -CF₃, -NO₂ or a halogen and R₁₁ is -H, or R₁₀ is -H and R₁₁ is -CF₃, or R₁₀ and R₁₁ are each independently a halogen.

34. The compound of Claim 33, with the proviso that when n is 1; X is -CH₂-; and one of R₃ or R₄ is -H; then the other of R₃ or R₄ is not -CH₂-R'', where R'' is selected from the group consisting of imidazol-5-yl, imidazol-5-yl independently substituted with one or more -CF₃, trihalomethyl, -NO₂ or halogen groups, 2,4-dihalo-[1H]-imidazol-5-yl and 2,4-diiodo-[1H]-imidazol-5-yl.

35. The compound of Claim 33 in which X is -CH₂-.

36. The compound of Claim 33 in which n is 1.

37. The compound of Claim 33 in which one of R_3 or R_4 is -H.

38. The compound of Claim 33 in which at least one of R_3 or R_4 is (C_1-C_6) alkyl, (C_2-C_6) alkenyl or (C_2-C_6) alkynyl.

39. The compound of Claim 38 in which X is $-CH_2-$ and n is 1.

40. The compound of Claim 38 which is Compound 9b.

41. The compound of Claim 33 in which R_3 and R_4 , taken together, are $-CH_2-(CH_2)_p-CH_2-$, where p is an integer from 0 to 6.

42. The compound of Claim 41 in which X is $-CH_2-$ and n is 1.

43. The compound of Claim 42 which is selected from the group consisting of Compound 10b and Compound 11b.

44. The compound of Claim 33 in which one of R_3 or R_4 is -H and the other is selected from the group consisting of $-(CH_2)_cOR'$, $-(CH_2)_cSR'$ and $-(CH_2)_cR_{12}$, where c is an integer from 1 to 3, R' is as previously defined and R_{12} is (C_5-C_{20}) aryl, substituted (C_5-C_{20}) aryl, 5-20 membered heteroaryl, substituted 5-20 membered heteroaryl, (C_6-C_{26}) arylalkyl, substituted (C_6-C_{26}) arylalkyl, 6-26 membered heteroarylalkyl or substituted 6-26 membered heteroarylalkyl,

with the proviso that R_{12} is other than imidazol-5-yl, imidazol-5-yl independently substituted with one or more $-CF_3$, trihalomethyl, $-NO_2$ or halogen groups, 2,4-dihalo-[1H]-imidazol-5-yl and 2,4-diiodo-[1H]-imidazol-5-yl.

45. The compound of Claim 44 in which R_3 -H; R_4 is selected from the group consisting of $-(CH_2)_cOR_{20}$ and $-(CH_2)_cSR_{20}$, where c is an integer from 1 to 3 and R_{20} is

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selected from the group consisting of (C₁-C₆) alkyl, (C₂-C₆) alkenyl and (C₂-C₆) alkynyl.

46. The compound of Claim 45 which is selected from the group consisting of Compound 7b and Compound 8b.

47. The compound of Claim 44 in which R' is -H or (C₁-C₄) alkyl and R₁₂ is pyrazolyl or indolyl.

48. The compound of Claim 47 which is selected from the group consisting of Compound 12b and Compound 13b.

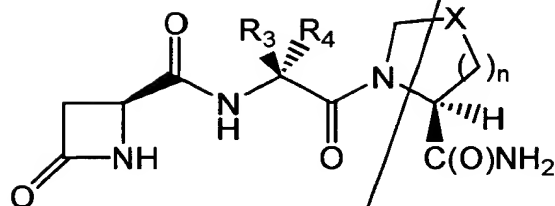
49. The compound of Claim 33 in which R₃ is -H and R₄ is -(CH₂)_i-R₂₁, where i is an integer from 0 to 4 and R₂₁ is a moiety which acts as a free-radical trap or inhibitor of NOS.

50. The compound of Claim 49 in which R₂₁ is a free-radical trap which is selected from the group consisting of di-t-butyl-hydroxyphenyl, 3,5-di-t-butyl-4-hydroxyphenyl, a tocopherol, 2,3-dihydro-5-hydroxy-2,2,4,6,7-pentamethyl benzofuran-3-yl, a nitron, 2,4-dioxo-isoquinolyl and 2,4-dioxo-isoquinol-3-yl,

or R₂₁ is an inhibitor of NOS which is selected from the group consisting of -NR₂₂-C(NR₂₂)-R₂₂, -NH-C(NH)-R₂₂, -NR₂₂-C(NR₂₂)-SR₂₂, -NR₂₂-C(NH)-SR₂₂, -NR₂₂-C(NR₂₂)-NR₂₂R₂₂ and -NH-C(NR₂₂)-NH₂, where each R₂₂ is independently selected from the group consisting of -H and (C₁-C₃) alkyl.

51. The compound of Claim 50 which is selected from the group consisting of Compounds 1b, 2b, 3b, 4b, 5b and 6b.

52. The compound of Claim 33 which has the structural formula:



wherein n, X, R₃ and R₄ are as previously defined.

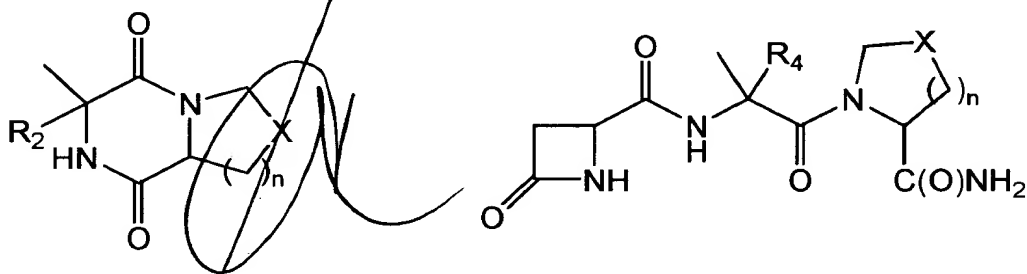
53. A compound having the formula:



or a pharmaceutically acceptable salt or hydrate thereof,
wherein:

-S-S- represents a disulfide bridge;

each r is independently an integer from 1 to 6; and A and B are each independently selected from the group consisting of:



wherein:

each n, which may be the same or different, is an integer from 0 to 3;

each X, which may be the same or different, is selected from the group consisting of -S-, -O-, -NR- and -CH₂-;

R₄ is selected from the group consisting of -H, -CN, -C(O)OR, -C(O)NRR, -C(NR)NRR, trihalomethyl, halogen, (C₁-C₆) alkyl, substituted (C₁-C₆) alkyl, (C₂-C₆) alkenyl, substituted (C₂-C₆) alkenyl, (C₂-C₆) alkynyl, substituted (C₂-C₆) alkynyl, (C₅-C₂₀) aryl, substituted (C₅-C₂₀) aryl, 5-20 membered heteroaryl, substituted 5-20 membered heteroaryl, (C₆-C₂₆) arylalkyl, substituted (C₆-C₂₆) arylalkyl, 6-26 membered heteroarylalkyl and substituted 6-26 membered heteroarylalkyl;

5 R₂ is selected from the group consisting of -H, -OR, -SR, -NRR, NO₂, -CN, -C(O)OR, -C(O)NRR, -C(NR)NRR, halogen, trihalomethyl, (C₁-C₆) alkyl, substituted (C₁-C₆) alkyl, (C₂-C₆) alkenyl, substituted (C₂-C₆) alkenyl, (C₂-C₆) alkynyl, substituted (C₂-C₆) alkynyl, (C₅-C₂₀) aryl, substituted (C₅-C₂₀) aryl, 5-20 membered heteroaryl, substituted 5-20 membered heteroaryl, (C₆-C₂₆) arylalkyl, substituted (C₆-C₂₆) arylalkyl, 6-26 membered heteroarylalkyl and substituted 6-26 membered heteroarylalkyl;

10 each alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl and the group consisting of -R, -OR, -SR, -NRR, -CN, -NO₂, -C(O)OR, -C(O)NRR, -C(S)NRR, -C(NR)NRR, -NR-C(NR)-R, -NR-C(NR)-OR, -NR-C(NR)-SR, -NR-C(NR)-NRR, halogen and trihalomethyl; and

15 each R is independently selected from the group consisting of -H, (C₁-C₆) alkyl, (C₂-C₆) alkenyl, (C₂-C₆) alkynyl, (C₅-C₂₀) aryl, (C₆-C₂₆) arylalkyl, 5-20 membered heteroaryl and 6-26 membered heteroarylalkyl.

20 54. The compound of Claim 53 in which each X is -CH₂- and each n is 1.

25 55. The compound of Claim 53 in which R₂ and R₄ are independently selected from the group consisting of -H, (C₂-C₆) alkenyl and (C₂-C₆) alkynyl.

56. The compound of Claim 53 which is Compound 14c.

30 57. A pharmaceutical composition comprising a compound according to Claim 33 and a pharmaceutically acceptable excipient, carrier or diluent.

35 58. The pharmaceutical composition of Claim 57 in which the compound is selected from the group consisting of Compounds 1b, 2b, 3b, 4b, 5b, 6b, 7b, 8b, 9b, 10b, 12b, and 13b.

59. A pharmaceutical composition comprising a compound according to Claim 53 and a pharmaceutically acceptable excipient, carrier or diluent.

5 60. The pharmaceutical composition of Claim 59 in which the compound is selected from the group consisting of Compounds 14c, 15c, and 16c.

10 61. A method of treating a neurological disorder or CNS injury, said method comprising the step of administering to a subject an effective amount of a compound according to Claim 33.

15 62. The method of Claim 61 in which the neurological disorder is caused by brain or spinal cord trauma.

63. The method of Claim 61 in which the cognitive function is memory.

20 64. The method of Claim 61 in which the compound is administered following acute or chronic brain injury.

25 65. The method of Claim 61 in which the compound is selected from the group consisting of Compounds 1b, 2b, 3b, 4b, 5b, 6b, 7b, 8b, 9b, 10b, 12b, and 13b.

30 66. A method of treating a neurological disorder or CNS injury, said method comprising the step of administering to a subject an effective amount of a compound according to Claim 53.

67. The method of Claim 66 in which the neurological disorder is caused by brain or spinal cord trauma.

35 68. The method of Claim 66 in which the cognitive function is memory.

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69. The method of Claim 66 in which the compound is administered following acute or chronic brain injury.

70. The method of Claim 66 in which the compound is selected from the group consisting of Compounds **14c**, **15c**, and **16c**.

71. The compound of Claim 1 in which R_1 is -H and R_2 is $-(CH_2)_1-R_{23}$, where 1 is an integer from 0 to 4 and R_{23} is a moiety which acts as a free-radical trap or inhibitor of NOS.

72. The compound of Claim 71 which is selected from the group consisting of Compounds **11a**, **12a**, **13a**, **14a**, **15a** and **16a**.

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